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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,759	07/24/2002	David Ian Cook	1871-133	7566

6449 7590 01/18/2005

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EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 01/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/049,759	COOK ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 July 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-41* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-7, drawn to a method of treatment comprising administering an effective amount of an agent that blocks an inhibitory feedback mechanism controlling the activity of an Na+ transport protein with *reduced activity* and restores ion composition of the cytosol of diseased cells.

Group II, claim(s) 8-12, drawn to a method of treatment comprising administering an effective amount of an agent that blocks an inhibitory feedback mechanism controlling the activity of an Na+ transport protein with *over activity* and restores ion composition of the cytosol of diseased cells.

Group III, claim(s) 13-16, drawn to a method of diagnosis of a human disease comprising isolating a sample of cells from a subject and assessing the sample for *reduced* activity of Na+ transport protein.

Group IV, claim(s) 13-16, drawn to a method of diagnosis of a human disease comprising isolating a sample of cells from a subject and assessing the sample for *over* activity of Na+ transport protein.

Group V, claim(s) 17, drawn to a method of diagnosis of a human disease comprising isolating a sample of cells from a subject and assessing the sample for *over* expression of the Na+ transport protein.

Group VI, claim(s) 17, drawn to a method of diagnosis of a human disease comprising isolating a sample of cells from a subject and assessing the sample for *under* expression of the Na+ transport protein.

Group VII, claim(s) 18-21, drawn to a method of diagnosis of human disease comprising isolating a genomic DNA sample from a subject and assessing the sample for the presence of a gene encoding a mutated product causative of the *reduced* activity of the Na+ transport protein.

Group VIII, claim(s) 18-21, drawn to a method of diagnosis of human disease comprising isolating a genomic DNA sample from a subject and assessing the sample for the presence of a gene encoding a mutated product causative of the *over* activity of the Na+ transport protein.

Group IX, claim(s) 22-26, 32-33, and 38, drawn to an isolated DNA molecule comprising a nucleotide sequence showing at least 75% homology to the nucleotide sequence shown as SEQ ID NO: 1.

Group X, claim(s) 27-33 and 38, drawn to an isolated DNA molecule comprising a nucleotide sequence showing at least 75% homology to the nucleotide sequence shown as SEQ ID NO: 3.

Group XI, claim(s) 34, drawn to an intracellular Na+ receptor comprising the amino acid sequence of SEQ ID NO: 2.

Group XII, claim(s) 35, drawn to an intracellular Na+ receptor comprising the amino acid sequence of SEQ ID NO: 4.

Group XIII, claim(s) 36-37, drawn to an antibody that binds the receptor of SEQ ID NO: 2.

Group XIV, claim(s) 36-37, drawn to an antibody that binds the receptor of SEQ ID NO: 4.

Group XV, claim(s) 37, drawn to a method for detecting agonist or antagonist agents of the receptor.

Group XVI, claim(s) 39, drawn to an isolated DNA molecule comprising a nucleotide sequence of SEQ ID NO: 5.

Group XVII, claim(s) 40, drawn to an isolated DNA molecule comprising a nucleotide sequence of SEQ ID NO: 6.

Group XVIII, claim(s) 41, drawn to an isolated DNA molecule comprising a nucleotide sequence of SEQ ID NO: 7.

2. The inventions listed as Groups I-XVII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Group I recites the special technical feature of administration of an effective amount of an agent that blocks an inhibitory feedback mechanism controlling the activity of an Na+ transport protein with *reduced activity* and restores ion composition of the cytosol of diseased cells, which is not required by the other methods of Groups II-VIII and XV.

Group II recites the special technical feature of administration of an effective amount of an agent that blocks an inhibitory feedback mechanism controlling the activity of an Na+ transport protein

with *over activity* and restores ion composition of the cytosol of diseased cells, which is not required by the other methods of Groups I, III-VIII and XV.

Group III recites the special technical feature of diagnosing a human disease comprising isolating a sample of cells from a subject and assessing the sample for *reduced activity* of Na+ transport protein, which is not required by the other methods of Groups I-II, IV-VIII, and XV.

Group IV recites the special technical feature of diagnosing a human disease comprising isolating a sample of cells from a subject and assessing the sample for *over activity* of Na+ transport protein, which is not required by the other methods of Groups I-III, V-VIII, and XV.

Group V recites the special technical feature of diagnosing a human disease comprising isolating a sample of cells from a subject and assessing the sample for *over expression* of the Na+ transport protein, which is not required by the other methods of Groups I-IV, VI-VIII and XV.

Group VI recites the special technical feature of diagnosing a human disease comprising isolating a sample of cells from a subject and assessing the sample for *under expression* of the Na+ transport protein, which is not required by the other methods of Groups I-V, VII-VIII, and XV.

Group VII recites the special technical feature of diagnosing a human disease comprising isolating a genomic DNA sample from a subject and assessing the sample for the presence of a gene encoding a mutated product causative of the *reduced activity* of the Na+ transport protein, which is not required by the other methods of Groups I-VI, VIII, and XV.

Group VIII recites the special technical feature of diagnosing a human disease comprising isolating a genomic DNA sample from a subject and assessing the sample for the presence of a gene encoding a mutated product causative of the *over activity* of the Na+ transport protein, which is not required by the other methods of Groups I-VII and XV.

Group IX recites the special technical feature of an isolated DNA molecule comprising a nucleotide sequence showing at least 75% homology to the nucleotide sequence shown as SEQ ID NO: 1, which is not required by the other products of Groups X-XIV and XVI-XVIII.

Group X recites the special technical feature of an isolated DNA molecule comprising a nucleotide sequence showing at least 75% homology to the nucleotide sequence shown as SEQ ID NO: 3, which is not required by the other products of Groups XI-XIV and XVI-XVIII.

Group XI recites the special technical feature of an intracellular Na+ receptor comprising the amino acid sequence of SEQ ID NO: 2, which is not required by the other products of Groups IX-X, XII-XIV, and XVI-XVIII.

Groups XII recites the special technical feature of an intracellular Na+ receptor comprising the amino acid sequence of SEQ ID NO: 4, which is not required by the other products of Groups IX-XI, XIII-XIV, and XVI-XVIII.

Group XIII recites the special technical feature of an antibody that binds the receptor of SEQ ID NO: 2, which is not required by the other products of Groups IX-XII, XIV, and XVI-XVIII.

Group XIV recites the special technical feature of an antibody that binds the receptor of SEQ ID NO: 4, which is not required by the other products of Groups VIII-XII and XVI-XVIII.

Group XV recites the special technical feature of detecting agonist or antagonist agents of the receptor, which is not required by the other methods of Groups I-VIII.

Group XVI recites the special technical feature of an isolated DNA molecule comprising a nucleotide sequence of SEQ ID NO: 5, which is not required by the other products of Groups IX-XIV and XVII-XVIII.

Group XVII recites the special technical feature of an isolated DNA molecule comprising a nucleotide sequence of SEQ ID NO: 6, which is not required by the other products of Groups IX-XIV, XVI, and XVIII.

Group XVIII recites the special technical feature of an isolated DNA molecule comprising a nucleotide sequence of SEQ ID NO: 7, which is not required by the other products of Groups IX-XIV and XVI-XVII.

3. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species of Na+ transport protein are as follows:

a. NHE1

b. NHE2

c. NHE3

d. the Na+-HCO_3 cotransporter

e. the Na+K+Cl transporter

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

4. The claims are deemed to correspond to the species listed above in the following manner:

2, 14, 20

The following claim(s) are generic: 1, 13, 19.

5. The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

The special technical feature of (a) is NHE1. This special technical feature is not shared by any of the other species.

6. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species of agent administered to a patient wherein the Na+ transport protein has reduced activity are as follows:

f. amiloride or amiloride analogs

g. a G-protein inhibitor

h. a ubiquitin protein ligase inhibitor

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

7. The claims are deemed to correspond to the species listed above in the following manner:

3-4, 6

The following claim(s) are generic: 1.

8. The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

The special technical feature of (f) amiloride or amiloride analogs. This special technical feature is not shared by any of the other species.

9. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species of agent administered to a patient wherein the Na+ transport protein has over activity are as follows:

i. gene therapy agents

j. intracellular Na+ receptor activators

k. G-protein activators

l. ubiquitin ligase activators

m. endocytosis triggering agents

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

10. The claims are deemed to correspond to the species listed above in the following manner: 9

The following claim(s) are generic: 8.

11. The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

The special technical feature of (i) is gene therapy agents. This special technical feature is not shared by any of the other species.

12. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species of human disease is as follows:

n. hypertension

o. renal failure

p. cardiac hypertrophy

q. cardiological syndrome X

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

13. The claims are deemed to correspond to the species listed above in the following manner:

21

The following claim(s) are generic: 1-20.

14. The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

The special technical feature of (n) is hypertension. This special technical feature is not shared by any of the other species.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process

claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

If Applicant elects one from Inventions I-VII, one species from the human disease group must be chosen to be considered fully responsive.

If Applicant elects one from Inventions I, III-IV, and VII-VIII, one species from the Na+ transport protein group must be chosen to be considered fully responsive.

If Applicant elects Invention I, one species from the agent group (wherein the Na+ transport protein has reduced activity) must be chosen to be considered fully responsive.

If Applicant elects Invention II, one species from the agent group (wherein the Na+ transport protein has over activity) must be chosen to be considered fully responsive.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BEB
Art Unit 1647
13 January 2005

Bridget E. Bunner